REMARKS

Applicants respectfully request entry of the amendments hereinabove, reconsideration of the Office Action mailed on February 12, 2003 and allowance of the application.

Claims 1-8 and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by Lee et al. (US 65122002 B2).

The rejection states that Lee teaches the co-administration of estrogen agonists/antagonists and a cGMP PDEv inhibitor (e.g., sildenafil) for the treatment of premature ejaculation (column 21, lines 19-23; claims 3 and 5). The rejection also states that the reference discloses that the cGMP PDEv inhibitors have an IC50 for PDEv at less than 100 nonomolar, more preferably, at less than 50 nanomolar, more preferably still at less than 10 nanomolar (column 23, lines 51-54); and the cGMP PDEv inhibitors are selective over PDEiii, more preferably over PDEIII, and PDEiv (column 23, lines 62-65). The rejection also states that the reference also discloses that the claimed composition is preferably administered in different dosage forms including oral administration (column 41, lines 21-23).

The rejection notes that since the instant claims recite "comprising" language, the reference clearly anticipates the claimed invention.

Applicants traverse the rejection of the claims (as amended) under 35 U.S.C. 102(e) in light of Lee et al.

The claims have been amended to recite that an estrogen agonist/antagonist is not co-administered. Applicants submit that this amendment is fully supported. Support for this amendment may be found in claim 1 as originally filed. In addition, Applicants submit that the literal basis for such amendment is not required to be found in the specification (the claim phrase need not be "*in haec verba*" in the specification *In Re Wright* 9 U.S.P.Q.2d 1649, 1651 (Fed. Cir. 1989); Crowne Operations, Int'l, Inc. v. Solutia, Inc. 289 F.3d 1367, 1376 (Fed. Cir. 2002). Applicant submits that it is well settled that an inventor may excise the prior art from the claim and still satisfy the written description requirement of

section 112, first paragraph *In re Johnson,* 194 U.S.P.Q.187 (C.C.P.A. 1977). Thus, it is a perfectly legitimate procedure for an inventor to claim less than the full scope of his disclosure since it is for an inventor to decide what bounds of protection he will seek (see *In re Wertheim* 191 U.S.P.Q. 90 (C.C.P.A. 1976)). See also In re Driscoll 195 U.S.P.Q. 434 CCPA 1977 which cites the following case.

Engineering Development Laboratories v. Radio Corp. of America 68 USPQ 238 241-242 (CA2 1946).

Judge Learned Hand

"If, when [applicants] yield any part of what they originally believed to be their due, they substitute a new "invention", only two courses will be open to them: they must at the outset either prophetically divine what the art contains, or they must lay down a barrage of claims, starting with the widest and proceeding by the successive incorporation of more and more detail, until all combinations have been exhausted which can by any possibility succeed. The first is an impossible task; the second is a custom already more honored in the breach than in the observance, and its extension would only increase that surfeit of verbiage whicfh has for long been the curse of patent practice, and has done much to discredit it. *It is impossible to imagine any public purpose which it could serve.[emphasis added]*

The Court of Appeals for the Federal Circuit, in ruling on the standard for anticipation under 35 U.S.C. §102(b), stated

> [i]t is elementary that an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice or device.

In re Donohue, 226 U.S.P.Q. 619, 621 (1985); and "...exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference." Atlas Power Co. v. E. I. duPont DeNemours & Co., 224 U.S.P.Q. 409, 411 (1984).

As amended Applicants submit that their claims are not anticipated since they exclude the co-administration of an estrogen agonist/antagonist.

Applicants also submit that their claims are not obvious in light of Lee et. al. since Applicants submit that Lee et. al. does not provide the motivation to utilize a PDE5 inhibitor (without co-administering an estrogen agonist/antagonist) to treat premature ejaculation. The only statement regarding the use of a PDE5 inhibitor

alone is provided on column 5, lines 32-39. "More recently cGMP PDE inhibitors capable of inhibiting type V phosphodiesterase (cGMP PDE_V) have been found to be effective for the treatment of impotence, importantly by oral administration. " Applicants submit that the treatment of impotence is quite different from the treatment of premature ejaculation. Applicants submit that there is no motivation to modify the teachings of Lee et al. to achieve Applicants' claimed invention. The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. "The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification." In re Laskowski, 10 U.S.P.Q.2d 1397, 1399 (Fed. Cir. 1989).

The rejection does not detail reasoning that provides the motivation to modify the prior art and thus the rejection does not present a *prima facie* case of obviousness.

Claims 1-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Wilson et al. (US 6403597 B1).

The rejection states that Wilson teaches the use of type V phosphodiesterase inhibitors such as sildenafil for treating premature ejaculation (abstract; column 4, lines 9-18; claims). The rejection also states that the reference also teaches the claimed oral administration (claims 15, 17-19, 21, 40-44 of US '597) as required in claim 8 and the claimed dosage amount of phosphodiesterase inhibitors (e.g., sildenafil citrate), in the range of about 1 mg to about 250 mg, typically in the range of about 15 mg. to about 100 mg (column 22, line 65 thru column 23, line 7), as required in claims 9-10.

The rejection states that although the reference is silent about "PDE5 inhibitor has an IC 50 against the PDE5 enzyme of less than 100 nanometer" in claim 3; "PDE5 inhibitor has selectivity over PDE3 of greater than 100 fold" in claim 4; "PDE5 inhibitor has selectivity over both PDE3 and PDE4 of greater than 100 fold" in claim 5; and "PDE5 inhibitor has an IC 50 against the PDE5 less than 100 nM and a selectivity over PDE3 of greater than 100 fold" in claim 6, such

characteristics or properties are deemed to be inherent to the composition, i.e., it was always there.

Applicants traverse the rejection of the claims (as amended) under 35 U.S.C. 102(e) in light of Wilson et al.

The claims have been amended to recite that the administration is oral. Applicants submit that this amendment is fully supported. Support for this amendment may be found in claim 8 as originally filed and page 11, line 9.

The Court of Appeals for the Federal Circuit, in ruling on the standard for anticipation under 35 U.S.C. §102(b), stated

> [i]t is elementary that an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice or device.

In re Donohue, 226 U.S.P.Q. 619, 621 (1985); and "...exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference." Atlas Power Co. v. E. I. duPont DeNemours & Co., 224 U.S.P.Q. 409, 411 (1984).

As amended Applicants submit that their claims are not anticipated since Wilson et al. does not teach the oral administration of a PDE5 inhibitor before Applicants' priority file date of November 20, 2000. Thus, Wilson et al. does not teach each element of the claimed invention. Specifically, while Wilson et al. application serial number 09/888,250 filed on June 21, 2001 does disclose the oral administration of a PDE5 inhibitor for the treatment of premature ejaculation, the parent application (Wilson et al. application serial no. 09/467,094 filed December 10, 1999) does not disclose the oral administration of a PDE5 inhibitor for the treatment of premature ejaculation. Accordingly, as of December 10, 1999 the only administration method was transmucosal (e.g., buccal, sublingual, rectal) application serial no. 09/467,094 page 8, line 29- page 9, line 8. Since Applicants' application has a filing date that is prior to the earliest Wilson et al. application that teaches oral administration Wilson et al. is not an effective reference under 35 U.S.C. 102(e). This is because the invention was not described in a patent that was filed prior to Applicants' invention thereof as evidenced by Applicants' November 20, 2000 priority filing date.

Applicants note that their claim term oral is not intended to encompass the terms buccally or sublingually as evidenced by their specification page 11, lines 9-10 which recite the terms oral, buccal and sublingual in the alternative.

Applicants also submit that their claims are not obvious in light of Wilson et. al. since Applicants submit that Wilson et. al. does not provide the motivation to administer a PDE5 inhibitor to treat premature ejaculation by an oral route. The 09/467,094 application is clearly directed to transmucosal administration routes and never suggests a different method of administration. Applicants submit that oral administration is quite different from transmucosal (buccal or sublingual) administration.

First, oral administration is unobvious in light of the Wilson et al which nowhere suggests oral administration. Second, Applicants strongly submit that by emphasizing local administration one skilled in the art would recognize that the reference impliedly teaches away from oral administration (the normal and preferred method of pharmaceutical administration). Restated, the only logical conclusion from Wilson et al.'s emphasis on local administration is that the normal preferred oral administration is not available as a mode of administration.

Applicants further submit that there is no motivation to modify the teachings of Wilson et al. to achieve Applicants claimed invention. The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. "The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification." In re Laskowski, 10 U.S.P.Q.2d 1397, 1399 (Fed. Cir. 1989).

The rejection does not detail reasoning that provides the motivation to modify the prior art and thus the rejection does not present a *prima facie* case of obviousness.

Again, oral administration is nowhere suggested or disclosed in Wilson et al. in animals or humans, and Applicants submit that the fact that a compound can be administered by a particular route for one indication does not necessarily mean that

that mode of administration will be useful for a different indication. In support of this argument, Appellants enclose a copy of the following Exhibit:

Exhibit A - Meinhardt et al. , Internat. J. Impot. Res, 1997, 9, 17-26.

With reference to the nonobviousness of oral administration, Exhibit A discloses (see page 21 bottom left column) that

"Several vasodilators have a relaxing effect on the corporal tissue when applied intracavernosally or even topically, but this effect is not obvious when these drugs are taken orally..." .

The above quotation demonstrates that just because a compound is known to be orally administrable for one indication does not automatically mean that it is administrable orally for other indications. Simply, because many vasodilators are known for oral administration that does not mean they will automatically work to relax corporal tissue via oral administration, as illustrated by the above quotation. Indeed in Meinhardt, compounds known for administration by one route were inappropriate for administration by a different route even for the same indication. The same argument applies with equal force to Applicants' compounds--just because they were known for oral administration for the treatment of cardiovascular condition or impotence, the conclusion that prior to Applicants' invention one would have believed there was a reasonable likelihood of success that they would work orally to treat premature ejaculation is unwarranted.

Further, even allowing, *arguendo*, that any such suggestion or motivation were found in Doherty, the references provide no reasonable expectation of success.

Thus, the law is emphatic that "obvious to try" is NOT the test of obviousness under 35 U.S.C. §103. American Hospital supply Corp. v. Travenol

Laboratories, Inc., 223 USPQ 577, 582 (Fed. Cir. 1984). The Federal Circuit has explained the proper test:

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out **and would have a reasonable likelihood of success**, viewed in light of the prior art. **Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure** (emphasis added).

In re Dow Chemical Co., 5 USPQ.2d 1529, 1531 (Fed. Clir. 1988); Amgen, Inc. V. Chugai Pharmaceutical Co. Ltd. 18 USPQ.2d 1016. 1022-23 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991).

In light of the arguments concerning the Meinhardt reference Doherty clearly provides no reasonable expectation or likelihood of success. Again, even if an argument could be made that the art provides a suggestion to explore the oral administration of PDE5 inhibitors to premature ejaculation, this amounts, perhaps, to inviting experimentation, i.e., to perhaps making testing a PDE5 more obvious to try, which again is manifestly not the proper standard for patentability.

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatenable over Doherty, Jr. et al. (US 6037346 A), if necessary, and further view of Crenshaw et al (US 5276042) and Crenshaw et al (5151448) and/or Bick (US 4940731).

The rejection states that Doherty teaches or suggests the use of a type V phosphodiesterase inhibitor (e.g., sildenafil, pyrazolopyrimidinone, zaprinast) for treating premature ejaculation, mainly in local administration. The rejection also states that the reference also teaches that a PDE5 inhibitor is given daily in the range of approximately 0.1 to 500 mg/day.

The rejection states that Crenshaw '042, '448 and '731 teach the use of antidepressants such as fluoxetine, paroxetine and/or sertraline for the treatment of premature ejaculation.

The rejection acknowledges that the teaching of Doherty differs from the claimed invention in the use of a PDE5 inhibitor in "normal erectile function" (claims 1-11) and in oral form (claim 8).

The rejection argues that although the reference is silent about the efficacy of PDE5 inhibitor in the treatment of premature ejaculation for a "normal erectile function" patient, one having ordinary skill in the art would have motivated to apply the claimed PDE5 inhibitor (e.g., sildenafil), with reasonable expectation of success, to treat patients with premature ejaculation regardless of normal erectile function or erectile dysfunction. The rejection states that one having ordinary skill in the art would have known that a PDE5 inhibitor would be effective in treating premature ejaculation in patients with "normal erectile function" as well as a erectile problem patient. The rejection reasons that the state of the premature ejaculation treatment art does not distinguish between a patient with "normal erectile function and a patient with an erectile function problem. The rejection also states that, rather the prior art generally teaches that any effective agent for the treatment of premature ejaculation would be effective in treating premature ejaculation regardless of "normal erectile function" or erectile problem. The rejection concludes that based on the state of the prior art, differences in "normal erectile function" will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such "normal erectile function" is critical.

Finally, the rejection states that the determination of dosage for having optimum therapeutic index is well considered within the skill of the artisan, absent evidence to the contrary.

Applicants traverse the rejection of the claims (as amended) under 35 U.S.C. 103 in light of Doherty, Jr. et al. (US 6037346 A), if necessary, and further in view of Crenshaw et al (US 5276042) and Crenshaw et al (5151448) and/or Bick (US 4940731).

The rejection interprets the art as teaching that the treatment of premature ejaculation would be effective in treating premature ejaculation regardless of "normal erectile function" or erectile problem yet provides no basis for this conclusion. The rejection provides a conclusionary statement regarding the prior art without providing specific basis for such conclusion. The basis for this conclusion must be based on a specific finding in the art. Without such specific finding the rejection is insufficient to make a prima facie case.

Again, the claims have been amended to recite that the administration is oral. Applicants submit that this amendment is fully supported. Support for this amendment may be found in claim 8 as originally filed and page 11, line 9.

Applicants submit that Doherty et al. does not disclose or suggest the oral administration of a PDE5 inhibitor. Doherty et al. is clearly directed to the local administration of a PDE5 inhibitor (see the Title, Abstract and specification). In particular, the definitions in column 6 are all directed to local modes of administration (e.g., transurethral, intracavernosal).

First, oral administration is unobvious in light of the Doherty which nowhere suggests oral administration. Second, Applicants strongly submit that by emphasizing local administration one skilled in the art would recognize that the reference impliedly teaches away from oral administration (the normal and preferred method of pharmaceutical administration). Restated, the only logical conclusion from Doherty's emphasis on local administration is that the normal preferred oral administration is not available as a mode of administration.

Applicants further submit that there is no motivation to modify the teachings of Doherty et al. to achieve Applicants claimed invention. The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. "The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification." In re Laskowski, 10 U.S.P.Q.2d 1397, 1399 (Fed. Cir. 1989).

The rejection does not detail reasoning that provides the motivation to modify the prior art and thus the rejection does not present a *prima facie* case of obviousness.

Again, oral administration is nowhere suggested or disclosed in the primary reference, in animals or humans, and Applicants submit that the fact that a compound can be administered by a particular route for one indication does not necessarily mean that that mode of administration will be useful for a different indication. In support of this argument, Appellants have enclosed a copy of the following Exhibit:

Exhibit A - Meinhardt et al. , Internat. J. Impot. Res, 1997, 9, 17-26.

With reference to the nonobviousness of oral administration, Exhibit A discloses (see page 21 bottom left column) that

"Several vasodilators have a relaxing effect on the corporal tissue when applied intracavernosally or even topically, but this effect is not obvious when these drugs are taken orally..." .

The above quotation demonstrates that just because a compound is known to be orally administrable for one indication does not automatically mean that it is administrable orally for other indications. Simply, because many vasodilators are known for oral administration that does not mean they will automatically work to relax corporal tissue via oral administration, as illustrated by the above quotation. Indeed in Meinhardt, compounds known for administration by one route were inappropriate for administration by a different route even for the same indication. The same argument applies with equal force to Applicants' compounds--just because they were known for oral administration for the treatment of cardiovascular condition or impotence, the conclusion that prior to Applicants' invention one would have believed there was a reasonable likelihood of success that they would work orally to treat premature ejaculation is unwarranted.

Further, even allowing, *arguendo*, that any such suggestion or motivation were found in Doherty, the references provide no reasonable expectation of success.

Thus, the law is emphatic that "obvious to try" is NOT the test of obviousness under 35 U.S.C. §103. American Hospital supply Corp. v. Travenol Laboratories, Inc., 223 USPQ 577, 582 (Fed. Cir. 1984). The Federal Circuit has explained the proper test:

> The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out **and would have a reasonable likelihood of success**, viewed in light of the prior art. **Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure** (emphasis added).

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Applicants request an early examination and allowance of the application.

Respectfully submitted,

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